CGRP-Related Treatments for Headache

With Stephen D. Silberstein, MD

What Is Most Significant About These New Treatments?

For the first time, we've developed a treatment for migraine based on what causes migraine. We had the concept that calcitonin gene-related peptide (CGRP) was involved in migraine pathogenesis and so created compounds that interact with CGRP, the monoclonal antibodies to the peptide or its receptor (Table). In clinical trials, we found the side-effect profile is similar to placebo with no signs of safety issues, including no cardiovascular safety concerns. This is especially significant because CGRP is a vasodilator. This suggests that there may be different classes of CGRP and CGRP receptors and creates an avenue for continued research.

There is also the question of whether or not to use antibodies with botulinum toxin A. The reason this is such an important question is that botulinum toxin A works upon the C fibers involved in the pain response, and those fibers contain CGRP. The antibodies work on CGRP after the C fibers release it or in the delta fibers, which suggests a possibility that the effect of the antibodies and botulinum toxin A could be additive or even synergistic. There are studies beginning to test whether or not this is the case.

TABLE. CALCITONIN GENE-RELATED DRUGS FOR TREATMENT OF MIGRAINE

Drug	Class	Route	Stage of Development
Erenumab-aooe	MAb to CGRP receptor	SC	Approved for migraine prevention May 2018
Eptinezumab	MAb to CGRP	IV	In development, ongoing phase 3 trials
Fremanezumab-vfrm	MAb to CGRP	SC	Approved for migraine prevention Sept 2018
Galcanezumab-gnlm	MAb to CGRP	SC	Approved for migraine prevention Sept 2018

Abbreviations: CGRP, calcitonin gene-related peptide; IV, intravenous; MAb, monoclonal antibody; SC, subcutaneous.

What Do Clinicians Need to Know?

We are subject to the whims of the insurance companies. For patients to be approved by insurance to receive the treatment, they have to have failed treatment with botulinum toxin or at least 2 medications for migraine. This means that clinicians cannot use it as first-line therapy unless the patient is able and willing to pay for the treatment. It is also important to keep in mind that we don't yet have data on long-term use of any of these drugs. Because I tend to be conservative about using new treatments, I don't think it is unreasonable to try other medications first, but if those don't work, then the approved CGRP-related drugs should be tried.

Women of child-bearing age should not use the newly approved CGRP-related drugs because these antibodies can be transported to a developing fetus. We don't know if that will be harmful, but we also don't have data showing that they will not cause harm.

What Do Patients Need to Know?

Some patients experience constipation after treatment with antibodies to the CGRP receptor. Interestingly, there is a patent to test a CGRP-related medication for the treatment of diarrhea. Although this side effect was bothersome for 1 or 2 patients who I've treated, it is generally mild, transient, and much less of a problem than the migraine being treated. I've told patients who experience constipation to increase dietary fiber (eg, eat prunes) to deal with the issue. ■

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